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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 13 1998

Warning Letter

Mr. Tofte Marlind, Managing Director
Stril AB
Finnhyttans Ind. Omrade
714 00 Kopparberg
SWEDEN

Dear Mr. Tofte:

During an inspection of your firm located in Kopparberg, Sweden on September 28-29, 1998, our investigator determined that your firm sterilizes endosseous implants. These products are medical devices as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for their manufacture, packing, storage, or installation are not in conformity with the Good Manufacturing Practice (GMP) requirements set forth in the Quality System Regulation (copy enclosed), as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

820.75(a ) and (c) Process validation.

Failure to validate with a high degree of assurance and approve a process according to established procedures, as required under 820.75(a); and,

Failure to review and evaluate the process and, where appropriate, perform revalidation when changes or process deviations occur, as required under 820.75(c).

For example, the Dose Validation Document establishes the scan width of [redacted] mm and the conveyor speed of [redacted] m/minute as the process parameters. However, the sterilization records for lots [redacted] and [redacted] reflect a scan width of [redacted] mm and conveyor speed of [redacted] and [redacted] m/minute. This is covered as Item #1 on the FDA 483 issued at the close of the inspection. The scan width reflected in the lots referenced were not validated as required by 820.75(a), which also means you are in violation of 820.75(c) because these changes in parameters from the validated parameters was not validated as required by 820.75(c) when changes or process deviations occur.

In addition, Item #5 on the FDA 483 states that the dose mapping study does not specify the maximum dose location. Our investigator's report indicates that Stril follows the European standard for E-beam validation, but the maximum dose location within the product load is not indicated, as recommended in the standard.

820.181(b) Device master record.

Failure to establish production process specifications, including the appropriate equipment specifications, as required under 820.181(b).

For example, the process specifications do not include allowable specification variations (i.e., lower and upper ranges) for the E-beam scan width and conveyor speed.

820.184 Device history record.

Failure of the Device History Record to demonstrate that the device is manufactured in accordance with the Device Master Record, as required under 820.184.

This charge is supported by Item #3 on the FDA 483 citing Stril for records illustrating that parameters used during routine sterilization do not match validated parameters.

820.80(d) Receiving, in-process, and finished device acceptance.

Failure to implement procedures for finished device acceptance to ensure that each production run, lot, or batch of finished devices meets acceptance criteria, as required in 820.80(d).

Item #6 on the FDA 483 states that the firm released lots without having calorimetric readings.

With regard to Item #2 on the FDA 483, one run is acceptable for purposes of performance qualification, and multiple runs are not necessary for validation of an E-beam sterilization process. However, it is important to recognize that the dose be suitable for the bioburden level and that a consistent dose be delivered. The process should be monitored during every production run to assure that the validated dose is delivered.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is Stril's responsibility to ensure adherence to each requirement of the Act and its implementing regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected.

Please notify this office in writing within 15 working days of receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Once Stril submits a response to the FDA outlining the corrections made to address the FDA 483 observations and the date(s) of implementation, a review will be completed of that response and a determination made as to whether the corrections appear adequate.

Your response should be sent to Sharon Kalokerinos, Dental, ENT and Ophthalmic Devices Branch, Division of Enforcement II, Office of Compliance at the letterhead address.

Sincerely yours,

Lillian J. Gill
Director
Office of Compliance
Center for Devices and Radiological Health

Enclosure
(As stated)